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EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/671,242	LEES ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-30,32-36 and 67-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30, 32-36, 67-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicant's amendment in response to office action dated April 21, 2006 filed on October 23, 2006 is acknowledged. Amendment to the specification is noted. Claims 1-24, 31 and 37-66 have been cancelled. Claims 25, 28 and 32 have been amended. New claims 67-82 have been added. Therefore, claims 25-30, 32-36 and 67-82 are under examination.

Response to Amendments and Remarks

Objection to Specification

The objection to the specification is withdrawn in the light of amendment to the specification.

Rejections - 35 USC § 112

The rejection of claim 31 under 35 U.S.C. 112, second paragraph is moot in view of cancellation of the claim.

The rejection of claims 25-30, 32-36 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of amendment to claims 25, 28 and 32.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-30, 32-36, and 67-82 stand/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific protein and sequence, does not reasonably provide enablement for all the LDL binding proteins, and any variant/analogs or fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope

with these claims. The claimed invention is directed to a method for identifying a candidate agent that binds to LBP-2 comprising contacting in vitro a candidate agent and LBP-2 polypeptide or a fragment or analog thereof. The specification, however, only discloses cursory conclusions to support the findings. See the discussion below.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those skilled in the art, 7) the predictability or unpredictability of the art and 8) the breadth of the claims.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The quantity of experimentation necessary:

In the instant case, the amount of experimentation is enormous since the number of changes from the specific sequence are large, one of skill in the art would have to make and test each one to determine if it had the LDL binding activity of the parent protein. The specification on pages17+ provides a discussion about the fragments/analogs. However, the specification fails to provide any detail as to the structure, size or function of the claimed fragment/analogs.

The amount of direction or guidance presented:

The LBP-2 polypeptide in claims 28 and 72 are directed to an amino acid sequence that binds to LDL and has at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 7 and SEQ ID NO: 43 respectively; claims 67 and 73 are identical to a fragment of at least 10 amino acid residues of SEQ ID NO: 7 and SEQ ID NO: 43 respectively; or claims 68 and 74differ by one or more conservative amino acid substitutions from the amino acid sequence of SEQ ID NO: 7 and SEQ ID NO: 43 respectively.

The specification while defining the analogs indicates at page 17, last paragraph that analogs of the invention exhibit at least 80%, preferably 90%, more preferably 95% or most preferably 98% homology with substantially the entire sequence of a naturally occurring LBP sequence, preferably with a segment of about 100 or 50, or 30, or 10, or 5, or 4, or 3 or 2 amino acid residues. However, the specification fails to demonstrate any analog that has at least 80%

identity to a portion of the sequence set forth in SEQ ID NO: 7 (claims 28, 67, 68) and SEQ ID NO: 43 (claims 72, 73, 74) which have the LDL binding activity. There is no guidance provided to allow the skilled artisan to predict the portion of the SEQ ID NO: 7 or SEQ ID NO: 43 that would have had at least 80%, 90% and 95% identity to the claimed peptide sequence fragment respectively..

Also the specification fails to describe or provide guidance about the peptide sequence having identity to a fragment of at least ten amino acid residues of SEQ NO: 7 (claims 28) and SEQ ID NO: 43 (claim 72). It is not clear to a skilled artisan that what is the position of these ten amino acids in relation to the amino acid sequence set forth in SEQ ID NO: 7 and SEQ ID NO: 43. Although Examples 8 and 9 (pages 47-50) demonstrate the binding of LBP-2 (full length) and LDL by Affinity Coelectrophoresis Assay (ACE), this is not demonstrative of any analogs that are claimed in claims 28 and 31. For these reasons it would require undue experimentation to make the claimed invention.

The specification indicates at page 18-19 and in Table 1 that preferred analogs include LBP or biologically active fragments thereof whose sequence differ from the wild type sequence by one or more conservative amino acid substitutions or by one or more non-conservative amino acid substitutions, deletions or insertions which do not abolish LBP biological activity. However, the specification fails to provide a variant, which has LBP biological activity. There is no disclosure about the biological activities of these claimed variants. Identification of the full length LDL binding polypeptide (Fig. 7A, SEQ ID NO: 43 and Fig. 7B, SEQ ID NO: 7) is described (see specification page 6 and 11) and exemplified in the specification (Example 8 and 9 LBP-1, LBP-2 or LBP-3), however the specification fails to provide any discussion of a variant of polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43 that retains the activity of the full length polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43. The amount of guidance presented is limited to the exact sequence. No discussion is present as to where the changes might be made to SEQ ID NO: 7 and SEQ ID NO: 43. An example of desirable guidance for a LDL binding protein would be disclosure of the binding domain, which is not present. There is no guidance as to how the functional fragments and variants of the claimed nucleic acid encoding the protein can be generated. The specification has provided no guidance to enable one of ordinary skill in the art to determine the positions in the protein, which are tolerant to change (e.g., by amino acid

deletions, insertions or substitutions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active variants that may be constructed, because no specific guidance has been given in the specification.

The presence or absence of working examples:

The working examples are exclusively drawn to making one full-length LDL binding protein (LBP-1, LBP-2 or LBP-3) and characterizing cDNAs encoding the full-length protein (Examples 8, 9), however, the specification does not provide a working Example that demonstrates the claimed method.

The nature of the invention:

The scope of the claims include numerous structural variants. The specification does not disclose what might be considered a "LDL binding" variants of the claims 28, 29 and 31 or provide any example of the same.

The predictability or unpredictability of the art:

The nature of the variation makes it entirely unpredictable what might be considered a variant before the isolation of such a sequence has actually taken place. The effect of one or a few conservative substitutions might be somewhat predictable, if the active areas of the molecule were known, but more changes than that are less predictable.

The breadth of the claims:

The breadth of the claims is very broad and encompasses an unspecified number of variants regarding the polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43 as biological active variants. Given the breadth of the claims in the invention, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to make and use the mutants/fragments/variants/analogs of broadly claimed group of LDL binding proteins. Such teachings are absent in the specification. The scope of the claims includes fragments, variants, analogs and mutants of polypeptide. However the specification does not provide the information on the structure and function of the claimed variants of the said polypeptide. The number of changes to result in a sequence with 80% identity to the starting sequence would, of course, be 20 changes per hundred amino acids. The effects on function of this many changes is clearly

unpredictable. Finally, these claims are very broad in the sense that a vast number of different proteins fall within the scope of the claims.

For these reasons, it would require undue experimentation for one of skill in the art to make and use the claimed invention.

The rejection (supra) was set forth in the previous office action. In response Applicants traverse the rejection. The reason for the traversal is the LDL-binding protein, LBP-2 is believed to be involved in the focal, irreversible binding of LDL to the arterial wall, an event that starts and sustains the atherosclerotic process (specification page 12, lines 17-21). Applicants arguments have been considered but not found persuasive because said involvement of LBP-2 is merely "believed," there is no description or demonstration in the specification to enable the skilled artisan to make and use the invention.

Further Applicants submit at page 9 of 'Response' that the teachings of the specification , combined with the knowledge of a person of ordinary skill in the art enabled a skilled artisan to make and use polypeptides containing the LDL-binding fragments and variants of LBP-2 recited in the claims. In response Applicants' attention is drawn to the rejection (supra) and previous office action. The specification on pages 17+ provides a discussion about the fragments/analogs. However, the specification fails to provide any detail as to the structure, size or function of the claimed fragment/analogs. Although Examples 8 and 9 (pages 47-50) demonstrate the binding of LBP-2 (full length) and LDL by Affinity Coelectrophoresis Assay (ACE), this is not demonstrative of any analogs of SEQ ID NO: 7 that are claimed in claims 28, 67, 68, 69, 70; and analogs of SEQ ID NO: 43that are claimed in claims 72, 73, 74, 75 and 76. For these reasons it would require undue experimentation to make the claimed invention. The specification does not disclose what might be considered a "LDL binding" variants of the claims 28, 29 and 69, 70 or provide any example of the same.

For these reasons, it would require undue experimentation for one of skill in the art to make and use the claimed invention. Therefore the rejection remains.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita Mitra, Ph.D.
January 27, 2007

JON WEBER
SUPERVISORY PATENT EXAMINER